

REMARKS

Claims 1-6, 8, and 10-11 are pending. Claims 7 and 9 have been cancelled. Applicants amend claim 5 to correct punctuation and amend claims 10 and 11 to focus on particular embodiments of the invention. Support for the amendments is found in the specification as originally filed. See, for example, page 22 lines 5 to 7, and page 17 lines 23 to 28. Applicants amend the title of the instant application to correct the spelling of "pyrrolidin-2-one."

The Office Action states that claim 11 is rejected under 35 U.S.C. §112, Second Paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, because the substituent "T" is not described in the claim. Applicants amend claim 11. In light of the amendment, Applicants respectfully request reconsideration and withdrawal of the rejection.

The Office Action states that claim 10 is rejected under 35 U.S.C. §112, First Paragraph, for lack of enablement, because the claim attempts to claim more than what is enabled in the disclosure. Applicants respectfully traverse the rejection. However, to further prosecution, Applicants amend claim 10. In light of the amendment, Applicants respectfully request reconsideration and withdrawal of the rejection.

The Office Action states that claims 1-6, 8, 10 and 11 are rejected under 35 U.S.C. §103(a) because the invention is rendered obvious over published patent application WO02/100830 A1 (Glaxo Group Ltd.). Applicants respectfully traverse the rejection. 35 U.S.C. §103(c)(1) provides, in pertinent part, that subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of §102 of title 35 U.S.C., shall not preclude patentability under §103 where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person. PCT/GB02/02721 (WO02/100830A1) published on December 19, 2002. The instant application claims priority to GB0228552.6 filed December 6, 2002 (i.e. the claimed invention was made on or before December 6, 2002). If PCT/GB02/02721 (WO02/100830A1) is prior art with respect to the instant application, it can only qualify as prior art under §102(e), since it was not a printed publication until after the date the claimed invention was made. Also, PCT/GB02/02721 and the instant application are both

owned by the same "person" (i.e. Glaxo Group Ltd.). Since PCT/GB02/02721 could only qualify as prior art under 35 USC §102(e), and PCT/GB02/02721 and the instant application are both owned by the same "person" (i.e. Glaxo Group Ltd.), PCT/GB02/02721 does not qualify as a prior art reference for purposes of §103(a) and cannot preclude patentability of the instant invention as provided by 35 USC §103(c)(1). Therefore, the rejection under 35 U.S.C. §103(a) is improper, and Applicants respectfully request withdrawal of the rejection.

The Office Action states the following obviousness-type double patenting rejections:

- (1) claims 1-6 and 8 are rejected over claims 1-9 of US Patent No. 7, 186,717 B2;
- (2) claims 1-6 and 8 are provisionally rejected over claim 1 of co-pending application 10/537,645;
- (3) claim 10 is provisionally rejected over claim 1 of co-pending application 11/548,402;
- (4) claim 11 is provisionally rejected over claim 3 of co-pending application 11/548,404;
- (5) claims 1-6 and 8 are provisionally rejected over claims 1-7 and 9 of co-pending application 11/548,395;
- (6) claims 1-6 and 8, 10 and 11 are provisionally rejected over claims 1-9, 12, 14 and 15 of co-pending application 11/378,947 (now granted as US 7,226,929 B2); and
- (7) claims 1-6, 8, 10 and 11 are provisionally rejected over claims 1-9, 12, 14 and 15 of co-pending application 11/384,094.

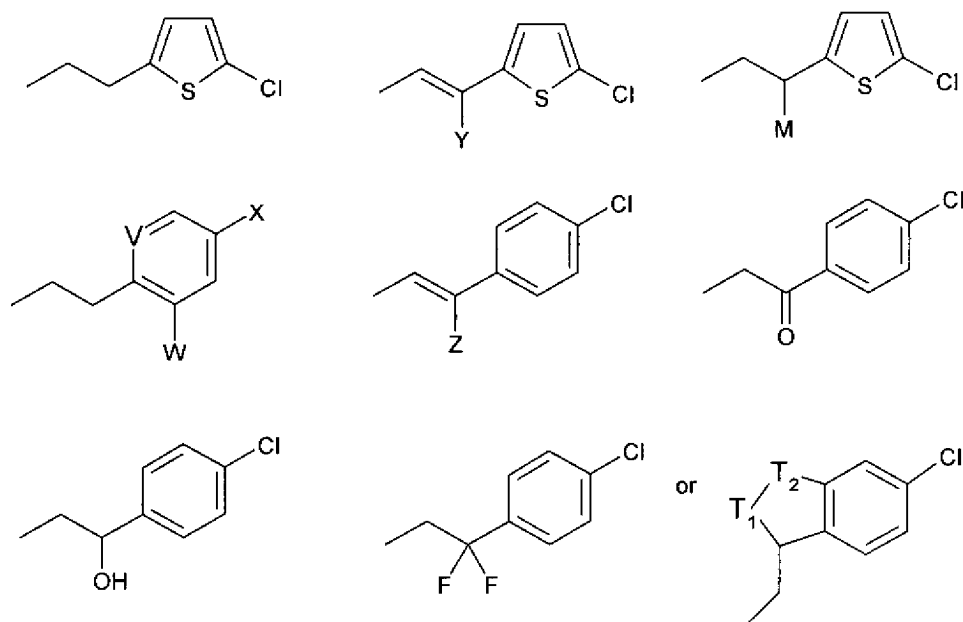
Applicants note that application 11/548,395 has now granted as US Patent No. 7,226,929 B2. Thus, Applicants address the rejection over 11/548,395 as a non-provisional rejection over claims 1-11 of US 7,226,929 B2.

MPEP§804(II)(B)(1) provides that a determination of obviousness for purposes of a double patenting rejection is "analogous to the nonobviousness requirement of 35 U.S.C. §103" yet the patent principally underlying the double patenting rejection is not prior art. Further, the Examiner has the burden of making factual determinations to support a conclusion of double patenting, demonstrating the differences between the conflicting claims, and providing the reasons why a person of ordinary skill in the art

would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent. For purposes of the following arguments, Applicants consider the pending claims in each co-pending application as of the date of this response.

The Office Action states for each provisional and non-provisional obviousness-type double patenting rejection that the only difference between the instant invention and the inventions disclosed in the publications is scope. Applicants agree that the scope of the instant invention as claimed is different from the scope of the claims of all of the cited patents and co-pending applications. However, Applicants respectfully submit that these differences are patentably distinct modifications rather than obvious variations.

(1) The Office Action states that claims 1-6 and 8 are rejected over claims 1-9 of US 7,186,717 B2. Applicants respectfully traverse the rejection. The compounds of the instant invention differ substantially from the invention as claimed in US 7,186,717 B2. For example, US 7,186,717 B2 claims a compound of formula (I) wherein "A" represents an optionally substituted thienyl(C₂₋₃)alkenylene. In comparison, the instant application claims a compound of formula (I) wherein "R⁶" is in the analogous position as "A," yet "R⁶" represents the following groups:



The differences between the substituents of "A" and those of "R⁶" are numerous. Furthermore, the pharmaceutical arts in general are unpredictable.

Therefore, the likelihood that any modification, especially those as substantial as the ones described above, would result in a compound that possesses the same properties, let alone additional advantageous properties, is uncertain. For example, the compounds of the instant invention possess Factor Xa inhibitory activity, but also unexpectedly possess thrombin inhibitory activity. Compounds as claimed in US 7,186,717 B2 possess less, if any, thrombin inhibitory activity when compared to the compounds of the instant invention. See, for example, page 117, lines 10-24 and the data therein relating to the ratio of thrombin inhibition to Factor Xa inhibition. Also, the Examiner has not provided reasons why one skilled in the art would be motivated to modify the invention as claimed in US 7,186,717 B2 to arrive at the instant invention, and conclude that the modifications are obvious variations.

(2) The Office Action also states that claims 1-6 and 8 are provisionally rejected for obviousness-type double patenting over claim 1 of co-pending application 10/537,645. Applicants respectfully traverse the rejection. Claim 1 of 10/537,645 is drawn to (E)-2-(5-chlorothiophen-2-yl)-N-[(3S)-1-[(1S)-1-methyl-2-morpholin-4-yl-2-oxoethyl]-2-oxopyrrolidin-3-yl]ethanesulfonamide in substantial crystalline form. Claims 1-6 and 8 of the instant application are drawn to compounds of formula(I) and subgenera thereof. The Office Action states that the compound of claim 1 of 10/537,645 is a species of formula(I) of the instant invention. Applicants respectfully submit that this assertion is incorrect. The genus of compounds of formula(I) of the instant invention does not encompass the species described in claim 1 of 10/537,645. Furthermore, the differences between the single species as claimed in 10/537,645 and the compounds of the instant invention are too numerous to even list. Applicants hereby reiterate the arguments above relating to the pharmaceutical arts in general. Additionally, the Examiner has not provided reasons why one skilled in the art would be motivated to modify the invention as claimed in claim 1 of 10/537,645 to arrive at the instant invention as claimed in claims 1-6 and 8, and conclude that the modifications are obvious variations.

(3) and (4) The Office Action states that claims 10 and 11 are provisionally rejected over claim 1 and 3 of co-pending applications 11/548,402 and 11/548,404, respectively. Applicants respectfully traverse the rejection. Claim 1 of 11/548,402 and claim 3 of 11/548,404 differ substantially from claims 10 and 11, respectively, of

the instant application. For example, the compounds of formula(I) described in claim 1 of 11/548,402 and claim 3 of 11/548,404 include the same substituents for "A" as those described above for "A" in US 7,186,717 B2. Claims 10 and 11 of the instant application comprise compounds of formula(I) wherein "R⁶" is as described in claim 1 of the instant application and as referenced above in (1). Thus, one example of how the instant invention as claimed in claims 10 and 11 differs from claim 1 and claim 3 of 11/548,402 and 11/548,404, respectively, is the differences among the substituent "A" and the substituent "R⁶." Such differences are substantial, and Applicants reiterate the aforementioned arguments regarding these differences, as well as the arguments relating to the pharmaceutical arts in general. Again, the Examiner has not provided reasons why one skilled in the art would be motivated to modify the invention as claimed in claim 1 of 11/548,402 and claim 3 of 11/548,404 to arrive at the instant invention as claimed in claims 10 and 11, respectively, and conclude that the modifications are obvious variations.

(5) The Office Action also states that claims 1-6 and 8 are provisionally rejected for obviousness-type double patenting over claims 1-7 and 9 of co-pending application 11/548,395. Applicants respectfully traverse the rejection. Applicants respectfully submit that claims 1-6 and 8 of the instant application differ substantially from claims 1-7 and 9 of co-pending application 11/548,395. For example, substituent "A" of co-pending application 11/548,395 is analogous to substituent "R⁶" of the instant invention. However, the scope of the definition of each substituent is substantially different. Substituent "A" of pending application 11/548,395 is an optionally substituted naphthylene, an optionally substituted phenyl(C₂₋₃)alkylene, or an optionally substituted phenyl(C₂₋₃)alkenylene, whereas "R⁶" of the instant invention is as described in paragraph (1) above. Furthermore, the scope of the definitions of substituents R² and R³ of the instant invention vary greatly from the definitions of the analogous substituents R² and R³ of the pending claims in co-pending application 11/548,395. For example, in claim 1 of 11/548,395, R² and R³ independently represent hydrogen, -C₁₋₃alkyl, or CF₃, with the proviso that one of R² and R³ is -C₁₋₃alkyl, or CF₃ and the other is hydrogen. However, substituents R² and R³ of the instant invention independently represent hydrogen, -C₁₋₆alkyl, -C₁₋₃alkylCN, -C₁₋₃alkylCO₂H, -C₁₋₄alkylOC₁₋₄alkyl, -C₁₋₄alkylS(O)_nC₁₋₄alkyl, -C₁₋₄alkylNR¹⁰R¹¹, -C₁₋

$_3\text{alkylINCO}_2\text{C}_{1-4}\text{alkyl}$, $-\text{C}_{1-3}\text{alkylCONR}^7\text{R}^8$, $-\text{C}_{1-3}\text{alkylCO}_2\text{C}_{0-2}\text{alkylR}^9$, $-\text{C}_{1-3}\text{alkylCOC}_{0-2}\text{alkylR}^9$, $-\text{C}_{1-3}\text{alkylCON}(\text{R}^8)\text{C}_{0-2}\text{alkylR}^9$, $-\text{C}_{1-3}\text{alkylINCO}_2\text{C}_{0-2}\text{alkylR}^9$, $-\text{C}_{1-3}\text{alkylINCOC}_{0-2}\text{alkylR}^9$ or $-\text{C}_{0-2}\text{alkylR}^9$, with the proviso that one of R^2 and R^3 is hydrogen and the other is a substituent other than hydrogen. Also, Applicants hereby reiterate the arguments above relating to the pharmaceutical arts in general. Again, the Examiner has not provided reasons why one skilled in the art would be motivated to modify the invention as claimed in claims 1-7 and 9 of co-pending application 11/548,395 to arrive at the instant invention as claimed in claims 1-6 and 8, and conclude that the modifications are obvious variations.

(6) and (7) The Office Action also states that claims 1-6, 8, 10 and 11 are provisionally rejected for obviousness-type double patenting over claims 1-9, 12, 14 and 15 of co-pending applications 11/378,947 and 11/384,094. Applicants wish to note that application 11/378,947 has now granted as claims 1-11 of US 7,226,929 B2, and co-pending application 11/384,094 has pending claims 1-6, 9, 10, 12, 14, and 16-18. In order to further prosecution, Applicants assume that the rejection is over claims 1-11 of US 7,226,929 B2 and claims 1-6, 9, 10, 12, 14, and 16-18 of co-pending application 11/384,094. Applicants respectfully traverse the rejection. The claims of US 7,226,929 B2 and co-pending application 11/384,094 vary substantially from those of the instant application. For example, in claim 1 of the instant application the substituent " R^6 " is as defined in paragraph (1) above, whereas the analogous substituent of " R^6 " of US 7,226,929 B2 and co-pending application 11/384,094 is an optionally substituted naphthyl (US 7,226,929 B2) or a fused bicyclic group as defined in claim 1 of 11/384,094. Additionally, " R^1 " of the instant invention as claimed in claim 1 is substantially different than the analogous " R^1 " substituent in US 7,226,929 B2, and co-pending application 11/384,094. For example, " R^1 " of the instant invention represents hydrogen, $\text{C}_{1-4}\text{alkyl}$, $-\text{CH}_2\text{CO}_2\text{H}$, $-\text{CH}_2\text{CO}_2\text{C}_{1-2}\text{alkyl}$, or $-\text{CH}_2\text{CONR}^7\text{R}^8$. " R^1 " of the compounds of formula (I) as claimed in claim 1 of both US 7,226,929 B2, and co-pending application 11/384,094 represents vastly different substituents including, *inter alia*, optionally substituted phenyl or aromatic heterocyclic groups, and alkylene, ankenylene, and alkynylene linked substituents represented by " W " as defined in US 7,226,929 B2, and co-pending application 11/384,094. Also, Applicants hereby reiterate the arguments

above relating to the pharmaceutical arts in general. Again, the Examiner has not provided reasons why one skilled in the art would be motivated to modify the invention as claimed in claims 1-11 of US 7,226,929 B2 and claims 1-6, 9, 10, 12, 14, and 16-18 of co-pending application 11/384,094 to arrive at the instant invention as claimed in claims 1-6 and 8, and conclude that the modifications are obvious variations.

Further, the Office Action states that "it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results" citing *In re Woods*, 582 F2d 638, 199 USPQ 137 (CCPA 1978). Applicants respectfully disagree with the Examiner's interpretation of the holding of *In re Woods*. Regardless, such statement has little relevance to the instant application. The differences between the instant invention and the claims in the cited patents and co-pending applications are more than a substitution of a methyl for a hydrogen. Therefore, Applicants decline to comment on the application of *In re Woods* to the instant application.

It appears that the Examiner agrees that the claims of US 7,186,717 B2, the pending claims of co-pending applications 10/537,645, 11/548,402, 11/548,404, 11/548,395, 11/384,094, and the claims of US 7,226,929 B2, fail to provide the reasons why a person of ordinary skill in the art would conclude that the invention defined in the claims of the instant application would have been an obvious variation of the invention(s) claimed in the cited patents and co-pending applications. See, for example, page 17 of the Office Action. The Examiner states that the prima facie case of obviousness is derived from the preferred teaching of the references in the "Best Mode" section of the patent applications. Applicants respectfully remind the Examiner that the cited patents and co-pending applications are not prior art. As provided in MPEP§804(II)(B)(1), "[w]hen considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art." Thus, the teachings in the specifications of the references are not available to support a prima facie case of obviousness. The conclusion of obviousness-type double patenting must be made in light of the factual determinations relative to the claims of the cited patents (and co-pending applications). The Examiner has failed to provide a factual basis for and reasons why one skilled in the art would conclude

that the instant invention as claimed is an obvious variation of the claimed inventions of the cited patents and co-pending applications. Therefore, the Examiner's assertion that the instant invention is an obvious variation of the claimed inventions of the cited patents and co-pending applications is merely conclusory. For the aforementioned reasons, the rejections are improper, and Applicants respectfully request reconsideration and withdrawal of the provisional and non-provisional obviousness-type double patenting rejections.

The Office Action states that claim 5 is objected to because there is not a period at the end of the claim. Applicants have added a period to claim 5. Applicants respectfully request reconsideration and withdrawal of the objection.

Applicants believe the present claims are in condition for allowance and such action is respectfully requested.

Should any other fees be deemed necessary to effect the timely filing of this paper, the Commissioner is hereby authorized to charge such fees to Deposit Account No. 07-1392.

If the Examiner has any outstanding issues with the pending claims, the Examiner is encouraged to telephone the undersigned at (919) 483-6334 for expeditious handling.

Respectfully submitted,



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***ELECTRONICALLY FILED USING THE EFS-WEB ELECTRONIC FILING SYSTEM OF THE UNITED STATES
PATENT & TRADEMARK OFFICE ON July 3, 2007.***